AOM in children

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ABSTRACT

INTRODUCTION: In the UK, about 30% of children under 3 years of age visit their GP each year with acute otitis media (AOM), and 97% of these receive antibiotics. In the US, AOM is the most common reason for outpatient antibiotic treatment. Without antibiotics, AOM resolves within 24 hours in about 60% of children, and within 3 days in about 80% of children. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for AOM in children; and what are the effects of interventions to prevent recurrence? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2010 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 29 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: analgesics, antibiotics, delayed antibiotics, immediate antibiotics, long-term antibiotic prophylaxis, longer courses of antibiotics, myringotomy, pneumococcal vaccination, tympanostomy with ventilation tubes, xylitol syrup or gum, and influenza vaccination.

QUESTIONS

INTERVENTIONS

Key points

- AOM is characterised by sudden onset of earache with a cloudy or bulging erythematous eardrum caused by middle-ear infection.

  Middle-ear effusion without signs of infection lasting >3 months suggests otitis media with effusion ('glue ear'), while chronic suppurative otitis media is characterised by continuing middle-ear inflammation and discharge through a perforated eardrum. These disorders are assessed in separate reviews in *Clinical Evidence*.

  The most common pathogens in AOM in the US and UK are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.

  In the UK, about 30% of children under 3 years of age visit their GP each year with AOM, and 97% of these receive antibiotics. In the US, AOM is the most common reason for outpatient antibiotic treatment.

- Without antibiotics, AOM resolves within 24 hours in about 60% of children, and within 3 days in about 80% of children.

  Analgesics and topical anaesthetics may reduce earache.

Antibiotics seem to reduce pain at 2 to 7 days, but they increase the risks of vomiting, diarrhoea, and rashes compared with placebo.

Immediate antibiotic use seems most beneficial in children aged <2 years with bilateral AOM and in children with AOM presenting with otorrhoea.

We do not know whether any one antibiotic regimen should be used in preference to another, although amoxicillin may be more effective than macrolides, and it should be considered as first-line treatment.

Longer courses of antibiotics reduce short-term treatment failure but have no benefit in the longer term compared with shorter regimens.

Immediate use of antibiotics may provide short-term reduction in some symptoms of AOM, but it increases the risk of diarrhoea and rashes compared with delayed treatment.

- Myringotomy seems less effective than antibiotics at reducing symptoms.
- We found limited evidence of only a short-term benefit from tympanostomy with ventilation tubes, with possibly increased risks of tympanosclerosis.
- Long-term antibiotic prophylaxis may reduce recurrence rates; however, the possibility of adverse effects and antibiotic resistance should be taken into account.

  We do not know whether any one regimen should be used in preference to another to prevent recurrent attacks.
- Vaccination in infancy with pneumococcal conjugate vaccine (PCV) has some effect on recurrent AOM.

  Vaccination with PCV in children aged 1 to 7 years does not reduce AOM recurrence.
- Influenza vaccine in healthy children has no effect on incidence of AOM.
- Xylitol given 5 times daily as prophylaxis has a small preventive effect on recurrent AOM, but the compliance issues in giving a medicine 5 times daily to such young children render it an unrealistic treatment option.

DEFINITION

Otitis media is an inflammation in the middle ear. Subcategories include acute otitis media (AOM), recurrent AOM, and chronic suppurative otitis media (CSOM). AOM is the presence of middle-ear effusion in conjunction with rapid onset of one or more signs or symptoms of inflammation of the middle ear. AOM presents with systemic and local signs, and it has a rapid onset. The diagnosis is made on the basis of signs and symptoms, principally earache in the presence of a cloudy or bulging eardrum (and immobility of the eardrum if pneumatic otoscopy is performed). Erythema is a moderately useful sign for helping to establish the diagnosis. If the eardrum has a normal colour, then risk of AOM is low. [1] Uncomplicated AOM is limited to the middle-ear cleft. [2] The persistence of an effusion beyond 3 months without signs of infection defines otitis media with effusion (also known as 'glue ear'; see review on otitis media with effusion), which can arise as a consequence of AOM, but can also occur independently. CSOM is characterised by continuing inflammation in the middle ear causing discharge (otorrhoea) through a perforated tympanic membrane (see review on CSOM). This review deals only with AOM in children.

INCIDENCE/ PREVALENCE

AOM is common, and has a high morbidity and low mortality in otherwise healthy children. In the UK, about 30% of children under 3 years visit their general practitioner with AOM each year, and 97% receive antimicrobial treatment. [3] By 3 months of age, 10% of children have had an episode of AOM. It is the most common reason for outpatient antimicrobial treatment in the US. [4]

AETIOLOGY/ RISK FACTORS

The most common bacterial causes of AOM in the US and UK are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. [3] Similar pathogens are found in Colombia. [5] There is some evidence that the predominant causative pathogen in recurrent AOM is changing from *Streptococcus pneumoniae* to *Haemophilus influenzae* after the release and widespread use of pneumococcal conjugate vaccine. [6] The established modifiable risk factors for recurrent AOM are the use of pacifiers, and care in daycare centres. Probable risk factors are privation of mother's milk, presence of siblings, craniofacial abnormalities, passive smoking, and presence of adenoids. [7]

PROGNOSIS

Without antibiotic treatment, AOM symptoms improve in 24 hours in about 60% of children, and in about 80% of children the condition resolves in about 3 days. Suppurative complications occur in about 0.12% of children if antibiotics are withheld. [8] Serious complications are rare in otherwise healthy children but include hearing loss, mastoiditis, meningitis, and recurrent attacks. [3] The WHO estimates that, in developing countries, 51,000 children aged <5 years die from complications of otitis media each year. [9]

AIMS OF INTERVENTION

To reduce the severity and duration of pain and other symptoms; to prevent complications; to minimise adverse effects of treatment.

OUTCOMES **Symptoms of AOM** (including pain [which can be assessed by surrogate measures such as parental observation of distress/crying and analgesic use], fever, middle-ear effusion, and otoscopic appearance); **recurrence of infection**, mastoiditis, and meningitis; **complications of infection** (including deafness), adverse effects of treatment.

METHODS *Clinical Evidence* search and appraisal September 2010. The following databases were used to identify studies for this systematic review: Medline 1966 to September 2010, Embase 1980 to September 2010, and The Cochrane Database of Systematic Reviews, August 2010 (online; 1966 to date of issue). This review was edited using The Cochrane Database of Systematic Reviews 2010, Issue 4. An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, and containing >20 individuals of whom >80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 29). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for AOM in children?

OPTION ANALGESICS

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Analgesics and topical anaesthetics may reduce earache compared with placebo.
- **Note:**
  A drug safety alert has been issued by the Food Drug Administration (FDA) on the risk of rare but serious skin reactions with paracetamol (acetaminophen).

Benefits and harms

Topical anaesthetic versus placebo:

We found one systematic review (search date 2009, 2 RCTs). [10]

Symptoms of AOM

Compared with placebo Topical anaesthetic drops may be more effective at reducing earache 10 to 30 minutes after administration in children taking paracetamol (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Pain					
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**25% reduction in ear ache , 10 minutes** 37/58 (64%) with topical anaesthetic drops 25/59 (42%) with placebo	RR 1.51 95% CI 1.06 to 2.15 P = 0.02 NNT 4 95% CI 3 to 27	●○○	topical anaesthetic drops

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		All participants also received paracetamol. See further information on studies for full details of co-interventions			
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**25% reduction in ear ache , 20 minutes** 46/58 (79%) with topical anaesthetic drops 35/59 (59%) with placebo All participants also received paracetamol. See further information on studies for full details of co-interventions	RR 1.34 95% CI 1.04 to 1.71 P = 0.02 NNT 5 95% CI 3 to 27	●○○	topical anaesthetic drops
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**25% reduction in ear ache , 30 minutes** 54/58 (93%) with topical anaesthetic drops 41/59 (69%) with placebo All participants also received paracetamol. See further information on studies for full details of co-interventions	RR 1.34 95% CI 1.12 to 1.61 P <0.002 NNT 5 95% CI 3 to 10	●○○	topical anaesthetic drops
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**50% reduction in ear ache , 10 minutes** 25/58 (43%) with topical anaesthetic drops 12/59 (20%) with placebo All participants also received paracetamol. See further information on studies for full details of co-interventions	RR 2.13 95% CI 1.19 to 3.80 P = 0.01 NNT 4 95% CI 3 to 16	●●○	topical anaesthetic drops
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**50% reduction in ear ache , 20 minutes** 34/58 (59%) with topical anaesthetic drops 28/59 (47%) with placebo All participants also received paracetamol. See further information on studies for full details of co-interventions	RR 1.24 95% CI 0.88 to 1.74 P = 0.22	⟷	Not significant
[10] Systematic review	117 people aged 3 to 19 years 2 RCTs in this analysis	**50% reduction in ear ache , 30 minutes** 49/58 (84%) with topical anaesthetic drops 35/59 (59%) with placebo All participants also received paracetamol. See further information on studies for full details of co-interventions	RR 1.43 95% CI 1.12 to 1.81 P = 0.003 NNT 4 95% CI 3 to 11	●○○	topical anaesthetic drops

Recurrence

No data from the following reference on this outcome. [10]

Complications

No data from the following reference on this outcome. [10]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[10] Systematic review	63 people aged 3 to 19 years Data from 1 RCT	**Adverse effects** with topical anaesthetic drops with placebo	One RCT in the review reported on adverse effects. The review reported that 3 people (treatment arm not specified) had mild dizziness that required no further treatment All participants also received paracetamol. See further information on studies for full details of co-interventions	○○○	

Oral analgesics versus placebo:

We found one RCT comparing the effects of treatment with ibuprofen or paracetamol three times daily versus placebo for 48 hours. [11]

Symptoms of AOM

Compared with placebo Oral ibuprofen or paracetamol may be more effective at reducing pain after 48 hours in children taking antibiotics (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Pain					
[11] RCT	219 children, aged 1 to 6 years with otoscopically diagnosed AOM and receiving antibiotic treatment with cefaclor for 7 days	**Incidence of ear ache , 2 days** 5/71 (7%) with ibuprofen 19/75 (25%) with placebo Parent assessed outcome	P <0.01	○○○	ibuprofen
[11] RCT	219 children, aged 1 to 6 years with otoscopically diagnosed AOM and receiving antibiotic treatment with cefaclor for 7 days	**Incidence of ear ache , 2 days** 7/73 (10%) with paracetamol 19/75 (25%) with placebo Parent assessed outcome	P value not reported Reported as non-significant	⟷	Not significant

Recurrence

No data from the following reference on this outcome. [11]

Complications

No data from the following reference on this outcome. [11]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[11] RCT	219 children, aged 1 to 6 years with otoscopically diagnosed AOM and receiving antibiotic treatment with cefaclor for 7 days	**Adverse effects (including mild nausea, vomiting, or abdominal pain)** 5/71 (7%) with ibuprofen 3/75 (4%) with placebo	Significance not assessed		
[11] RCT	219 children, aged 1 to 6 years with otoscopically diagnosed AOM and receiving antibiotic treatment with cefaclor for 7 days	**Adverse effects (including mild nausea, vomiting, or abdominal pain)** 3/73 (4.1%) with paracetamol 3/75 (4.0%) with placebo	Significance not assessed		

Further information on studies

[11] The evidence from this RCT is limited because the assessment of the child's pain relief was based on parental observation using a scale of 0 or 1.

[10] The review included studies in which participants were also given oral analgesics. It is therefore difficult to properly assess the real effects of the anaesthetic ear drops.

Comment: None.

OPTION ANTIBIOTICS VERSUS PLACEBO

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Antibiotics may lead to more rapid reduction in symptoms of AOM, but they increase the risk of adverse effects.
- Antibiotics seem to reduce pain at 2 to 7 days, but they increase the risks of vomiting, diarrhoea, and rashes compared with placebo.
- Antibiotics seem most effective in children aged <2 years with bilateral AOM and in children with AOM presenting with otorrhoea.

Benefits and harms

Antibiotics versus placebo:

We found 4 systematic reviews (search dates 1997, [12] 2008, [13] and 2005 [14] [15]).

Symptoms of AOM

Compared with placebo Antibiotics may be more effective at reducing pain and other symptoms of AOM after 2 to 14 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[12] Systematic review	741 children aged <2 years 4 RCTs in this analysis	**Symptomatic improvement , 7 days** 357/416 (86%) with antibiotics 277/325 (85%) with placebo alone or versus placebo plus myringotomy Antibiotic treatment included penicillins, sulphonamide, amoxicillin–clavulanic acid (co-amoxiclav) See further information on studies for definitions of AOM in trials	OR 1.31 (weighted OR, Mantel–Haenszel) 95% CI 0.83 to 2.08	⟷	Not significant
[13] Systematic review	2791 children aged 6 months to 15 years 9 RCTs in this analysis	**Pain , 2 to 7 days** 228/1425 (16%) with erythromycin, penicillins, sulphonamides 303/1366 (22%) with placebo Pain was assessed using parental report/score card/diary or clinician assessment at 4 days	ARR 6% 95% CI 4% to 9% RR 0.72 95% CI 0.19 to 0.40 P <0.001 NNT 16 95% CI 11 to 25	●○○	antibiotics
[13] Systematic review	1229 children aged 6 months to 15 years 4 RCTs in this analysis	**Pain outcomes , 24 hours** 223/624 (36%) with antibiotics 241/605 (40%) with placebo	RR 0.90 95% CI 0.78 to 1.04	⟷	Not significant
[15] Systematic review	273 children <2 years with bilateral AOM 6 RCTs in this analysis Subgroup analysis	**Pain, fever, or both , 3 to 7 days** 42/140 (30%) with antibiotics 74/133 (55%) with placebo	RR 0.64 95% CI 0.62 to 0.80 The differences for children aged <2 years with unilateral AOM and in children >2 years with unilateral or bilateral AOM were not significant	●○○	antibiotics
[15] Systematic review	116 children aged 6 months to 12 years presenting with otorrhoea 6 RCTs in this analysis Subgroup analysis	**Pain, fever, or both , 3 to 7 days** 12/50 (24%) with antibiotics 39/66 (60%) with placebo	RR 0.52 95% CI 0.37 to 0.73 P = 0.04	●○○	antibiotics

No data from the following reference on this outcome. [14]

Recurrence

Compared with placebo Antibiotics are no more effective at reducing the rate of recurrence in children with AOM (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[13] Systematic review	2153 people aged 6 months to 15 years 6 RCTs in this analysis	**Recurrence** 214/1113 (19%) with penicillins 214/1040 (21%) with placebo	RR 0.93 95% CI 0.79 to 1.10	⟷	Not significant

No data from the following reference on this outcome. [12] [14] [15]

Complications

Compared with placebo Antibiotics seem no more effective at reducing the risk of abnormal tympanometry at 1 and 3 months in children with AOM (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Abnormal tympanometry					
[13] Systematic review	808 children aged 6 months to 10 years 3 RCTs in this analysis	**Abnormal tympanometry , 3 months** 96/410 (23%) with antibiotics 96/460 (24%) with placebo	RR 0.97 95% CI 0.76 to 1.24 P = 0.81	⟷	Not significant
[13] Systematic review	927 children aged 6 months to 12 years 4 RCTs in this analysis	**Abnormal tympanometry , 1 month** 153/467 (33%) with antibiotics 168/460 (37%) with placebo	RR 0.89 95% CI 0.75 to 1.07 P = 0.21	⟷	Not significant
[14] Systematic review	1328 children aged 6 months to 12 years 5 RCTs in this analysis	**Abnormal tympanometry , 1 month** 47% with antibiotics 51% with placebo or no treatment Absolute numbers not reported	RR 0.93 95% CI 0.82 to 1.04	⟷	Not significant

No data from the following reference on this outcome. [12] [15]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[13] Systematic review	1401 children, aged 6 months to 15 years 5 RCTs in this analysis	**Adverse effects, including vomiting, diarrhoea, or rashes** 110/690 (16%) with antibiotics 83/711 (11%) with placebo	RR 1.38 95% CI 1.09 to 1.76 P = 0.008 NNH 24 95% CI 9 to 152	●○○	placebo

No data from the following reference on this outcome. [12] [14] [15]

Further information on studies

[12] Three RCTs based diagnosis of AOM on otoscopic appearance of the tympanic membrane and clinical signs of acute infection, and one RCT based diagnosis on otoscopy findings alone.

Comment: None.

Clinical guide:
The results of systematic reviews comparing antibiotics versus placebo may vary owing to differences in entry criteria and outcome measures. One quasi-randomised trial from Sweden conducted in 1954 comparing the effects of antibiotics versus placebo found no cases of mastoiditis in the penicillin-treated group, whereas 17% of the control group developed mastoiditis. [16] Therefore, in populations in which the incidence of complicating mastoiditis is high, antibiotic treatment would be advised.

OPTION CHOICE OF ANTIBIOTIC REGIMEN

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- We do not know whether any one antibiotic regimen should be used in preference to another, but amoxicillin may be more effective than macrolides, and it should be considered as first-line treatment.
- **Note**
  Antibiotics increase the risk of vomiting, diarrhoea, and rashes compared with placebo, but rates may vary between different types of antibiotic.

Benefits and harms

Different antibiotics versus each other:

We found three systematic reviews (search dates 1992, [17] 1999, [2] and 2008 [18]).

Symptoms of AOM

Different antibiotics compared with each other Macrolide antibiotics may be less effective than amoxicillin or amoxicillin–clavulanic acid (co-amoxiclav) at reducing signs and symptoms of AOM after 7 to 14 days, while other antibiotics may be as effective as each other (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[17] Systematic review	4580 children aged 4 months to 18 years 27 RCTs in this analysis	**Primary control defined as absence of any symptom or sign , 7 to 14 days** with with Absolute numbers not reported The review reported comparisons of a range of antibiotics, including ampicillin, amoxicillin, ceflacor, cefixime, amoxicillin–clavulanic acid (co-amoxiclav), erythromycin, penicillin, and sulfafurazole	P values not reported Reported as not significant for all comparisons	⟷	Not significant
[2] Systematic review	491 children, aged 4 weeks to 18 years 3 RCTs in this analysis	**Clinical failure rate , 7 to 14 days** with penicillin with ampicillin or amoxicillin Absolute results not reported	Clinical failure rate difference: +4.5% 95% CI –1.8% to +10.7%	⟷	Not significant
[2] Systematic review	185 children, aged 4 weeks to 18 years 4 RCTs in this analysis	**Clinical failure rates , 3 to 7 days** with cefaclor with ampicillin or amoxicillin Absolute numbers not reported	Clinical failure rate difference –5.4% 95% CI –15.2% to +4.4%	⟷	Not significant
[18] Systematic review	2766 children aged 6 months to 15 years 10 RCTs in this analysis	**Clinical failure , 10 to 16 days** 146/1371 (11%) with amoxicillin or amoxicillin–clavulanic acid 196/1395 (14%) with macrolide antibiotics	RR 1.31 95% CI 1.07 to 1.60 P = 0.008	●○○	amoxicillin or amoxicillin–clavulanic acid

Recurrence

No data from the following reference on this outcome. [2] [17] [18]

Complications

No data from the following reference on this outcome. [2] [17] [18]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[2] Systematic review	1518 patients aged 4 weeks to 18 years 5 RCTs in this analysis	**Diarrhoea** with cefixime with amoxicillin or ampicillin Absolute numbers not reported	ARI 8.4% 95% CI 3.8% to 13.1% NNH 12 95% CI 8 to 27	○○○	amoxicillin or ampicillin
[2] Systematic review	1366 patients aged 4 weeks to 18 years 3 RCTs in this analysis	**Gastrointestinal adverse effects** with amoxicillin–clavulanic acid (co-amoxiclav) with azithromycin Absolute numbers not reported	ARI 18% 95% CI 8% to 28% NNH 6 95% CI 4 to 13	○○○	azithromycin
[18] Systematic review	2766 children aged 6 months to 15 years 10 RCTs in this analysis	**Adverse effects** with amoxicillin or amoxicillin–clavulanic acid with macrolide antibiotics Absolute numbers not reported	RR 0.74 95% CI 0.60 to 0.90 P = 0.003	●○○	macrolide antibiotics

No data from the following reference on this outcome. [17]

Further information on studies

[2] Clinical failure was defined as the presence of pain, fever, middle-ear effusion, clinical signs of otitis media, or suppurative complications such as mastoiditis.

[17] AOM was defined as bulging or opacification of the tympanic membrane with or without erythema, accompanied by at least one sign (fever, ear ache, irritability, otorrhoea, lethargy, anorexia, vomiting, diarrhoea, poor or absent mobility of the tympanic membrane). Treatment success was defined as absence of all presenting signs and symptoms of AOM at the evaluation point closest to 7 to 14 days after start of treatment.

Comment: **Clinical guide:**
Many RCTs have studied a variety of antibiotic regimens for the treatment of otitis media, but there is heterogeneity in participants, treatment regimens, controls, and outcome measures.

OPTION IMMEDIATE VERSUS DELAYED ANTIBIOTIC TREATMENT

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Immediate use of antibiotics may provide short-term reduction for some symptoms of AOM, but it increases the risk of rashes and diarrhoea compared with delayed treatment.

Benefits and harms

Immediate versus delayed antibiotic treatment:

We found one systematic review (search date 2009). [19] Owing to heterogeneity among studies, the review did not perform meta-analyses, so we report data from individual RCTs here.

Symptoms of AOM

Immediate antibiotics compared with delayed antibiotics Immediate antibiotics may be more effective at reducing pain and other symptoms of AOM at 3 days, but not after 7 days (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[19] Systematic review	212 children aged 6 months to 10 years Data from 1 RCT	**Proportion of children with pain , 3 days** 28/111 (25%) with delayed antibiotics 15/101 (15%) with immediate antibiotics	OR 1.93 95% CI 0.96 to 3.88	⟷	Not significant
[19] Systematic review	212 children aged 6 months to 10 years Data from 1 RCT	**Proportion of children with pain , 7 days** 3/111 (3%) with delayed antibiotics 0/101 (0%) with immediate antibiotics	OR 6.55 95% CI 0.33 to 128.34	⟷	Not significant
[19] Systematic review	285 children aged 6 months to 10 years Data from 1 RCT	**Proportion of children with malaise , 3 days** 45/150 (30%) with delayed antibiotics 19/135 (14%) with immediate antibiotics	OR 2.62 95% CI 1.44 to 4.76	●●○	immediate antibiotics
[19] Systematic review	213 children aged 6 months to 10 years Data from 1 RCT	**Mean pain severity , 3 days** 2.56 with delayed antibiotics 1.81 with immediate antibiotics	Mean difference 0.75 95% CI 0.26 to 1.24	○○○	immediate antibiotics
[19] Systematic review	212 children aged 6 months to 10 years Data from 1 RCT	**Mean pain severity , 7 days** 1.17 with delayed antibiotics 1.05 with immediate antibiotics	Mean difference +0.12 95% CI –0.04 to +0.28	⟷	Not significant
[19] Systematic review	282 children aged 6 months to 12 years Data from 1 RCT	**Mean number of spoons of paracetamol/day** 2.28 with delayed antibiotics 1.69 with immediate antibiotics	Mean difference 0.59 95% CI 0.25 to 0.93	○○○	immediate antibiotics
[19] Systematic review	265 children aged 6 months to 12 years Data from 1 RCT	**Fever , days 4 to 6** 42/132 (32%) with delayed antibiotics 46/133 (35%) with immediate antibiotics	OR 0.88 95% CI 0.53 to 1.47	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[19] Systematic review	265 children aged 6 months to 12 years Data from 1 RCT	**Proportion of children with pain , days 4 to 6** 85/132 (64%) with delayed antibiotics 89/133 (67%) with immediate antibiotics	OR 0.89 95% CI 0.54 to 1.48	⟷	Not significant
[19] Systematic review	265 children aged 6 months to 12 years Data from 1 RCT	**Use of paracetamol or ibuprofen** 123/132 (93%) with delayed antibiotics 120/133 (90%) with immediate antibiotics	OR 1.48 95% CI 0.61 to 3.59	⟷	Not significant
[19] Systematic review	265 children aged 6 months to 12 years Data from 1 RCT	**Re-consultation rate** 13/132 (10%) with delayed antibiotics 11/133 (8%) with immediate antibiotics	OR 1.21 95% CI 0.52 to 2.81	⟷	Not significant

Recurrence

No data from the following reference on this outcome. [19]

Complications

No data from the following reference on this outcome. [19]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[19] Systematic review	285 children aged between 6 months and 12 years Data from 1 RCT	**Rash** 8/150 (5%) with delayed antibiotics 14/150 (9%) with immediate antibiotics	OR 1.21 95% CI 0.41 to 2.58	⟷	Not significant
[19] Systematic review	265 children aged between 6 months and 12 years Data from 1 RCT	**Diarrhoea** 10/132 (8%) with delayed antibiotics 31/133 (23%) with immediate antibiotics	OR 0.27 95% CI 0.13 to 0.58	●●○	delayed antibiotics
[19] Systematic review	265 children aged between 6 months and 12 years Data from 1 RCT	**Vomiting** 15/132 (11.4%) with delayed antibiotics 15/133 (11.3%) with immediate antibiotics	OR 1.01 95% CI 0.47 to 2.16	⟷	Not significant

Further information on studies

Comment: Prescribing delayed antibiotics, using a prescription to be filled later if symptoms do not improve, is a tool for the physician to reduce antibiotic use rather than a treatment option for AOM. If antibiotics have a small effect on the outcome of AOM, then this effect will clearly apply to immediate antibiotics. Because the evidence suggests that antibiotics should only be prescribed to certain subgroups of patients (children aged <2 years with bilateral AOM and children with AOM presenting with otorrhoea), physicians should discuss the wait-and-see policy with parents of children not in those subgroups. A delayed prescription should be provided with care, since oral antibiotics may not always be the best option in very young children with worsening symptoms. In these cases the physician and not the parents of the child should make the decision about whether to give antibiotics. In most developed countries, it is relatively easy for parents to re-consult a physician when symptoms either do not improve or get worse.

One study in the review showed no difference in re-consultation rate between the two groups. [19] One study comparing delayed antibiotics versus no antibiotics showed no difference in the outcomes of pain and fever. [20]

OPTION LONGER VERSUS SHORTER COURSES OF ANTIBIOTICS

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Longer courses of antibiotics reduce short-term treatment failure, but have no benefit over the longer term compared with shorter regimens.

Benefits and harms

Longer versus shorter course of antibiotics:

We found one systematic review (search date 2009). [21]

Symptoms of AOM

Longer courses of antibiotics compared with shorter courses Longer (8–10 days) courses of antibiotics are more effective at reducing symptoms and preventing relapse or re-infection at 8 to 19 days compared with 7-day courses, but are no more effective than shorter courses after 20 to 30 days (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[21] Systematic review	5093 children aged between 4 weeks and 15 years 16 RCTs in this analysis	**Treatment failure , 1 month or less** 486/2376 (20%) with short-course antibiotics (<7 days) 475/2717 (17%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 1.34 95% CI 1.15 to 1.55 P = 0.0001	●○○	longer-course antibiotics
[21] Systematic review	3932 children aged between 4 weeks and 15 years 11 RCTs in this analysis	**Treatment failure , 8 to 19 days** 340/1892 (18%) with short-course antibiotics (<7 days) 293/2040 (14%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 1.37 95% CI 1.15 to 1.64 P = 0.0004	●○○	longer-course antibiotics

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[21] Systematic review	2475 children aged between 4 weeks and 15 years 9 RCTs in this analysis	**Treatment failure , 20 to 30 days** 238/1141 (21%) with short-course antibiotics (<7 days) 271/1335 (20%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 1.16 95% CI 0.94 to 1.42	⟷	Not significant
[21] Systematic review	2068 children aged between 4 weeks and 15 years 7 RCTs in this analysis	**Treatment failure , 3 months or less** 391/973 (40%) with short-course antibiotics (<7 days) 399/1095 (36%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 1.18 95% CI 0.98 to 1.41	⟷	Not significant
[21] Systematic review	570 children aged between 4 weeks and 2 years 5 RCTs in this analysis	**Treatment failure , 1 month or less** 99/296 (33%) with short-course antibiotics (<7 days) 85/274 (31%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 1.09 95% CI 0.76 to 1.57	⟷	Not significant
[21] Systematic review	1064 children aged between 2 years and 15 years 6 RCTs in this analysis	**Treatment failure , 1 month or less** 74/530 (14%) with short-course antibiotics (<7 days) 86/534 (16%) with longer-course antibiotics (8–10 days) See further information on studies for definition of treatment failure	OR 0.85 95% CI 0.60 to 1.21	⟷	Not significant

Recurrence

No data from the following reference on this outcome. [21]

Complications

No data from the following reference on this outcome. [21]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Gastrointestinal adverse effects					
[21] Systematic review	4918 children aged between 4 weeks years and 15 years 13 RCTs in this analysis	**Gastrointestinal adverse effects** 206/2221 (9%) with short-course antibiotics (<7 days) 369/2697 (14%) with longer-course antibiotics (8–10 days)	OR 0.72 95% CI 0.60 to 0.87	●○○	short-course antibiotics (<7 days)

Further information on studies

[21] Treatment failure was defined as lack of clinical resolution, relapse, or recurrence of AOM during a 1-month period following the initiation of therapy. Clinical resolution was defined as improved or resolving signs or symptoms of AOM. Treatment failure at 3 months was defined as relapses and recurrences up to 3 months.

Comment: A subgroup analysis showed that children aged <2 years had no benefit from longer courses of antibiotics compared with shorter courses. In addition, they had a greater risk of treatment failure compared with older children irrespective of treatment duration. [21]

OPTION MYRINGOTOMY

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Myringotomy seems less effective than antibiotics at reducing symptoms.
- **Adverse effects**
  Myringotomy may be less likely than antibiotics to cause diarrhoea.

Benefits and harms

Myringotomy versus no myringotomy:

We found one RCT. [22]

Symptoms of AOM

Compared with no myringotomy Myringotomy may be no more effective than no myringotomy at reducing the symptoms of AOM after 1 to 7 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[22] RCT **4-armed trial**	171 children, aged 2 to 12 years with AOM The third arm evaluated amoxicillin (250 mg three times daily for 7 days) only The fourth arm evaluated amoxicillin plus myringotomy	**Pain , 24 hours** 26/36 (72.2%) with myringotomy only 29/40 (72.5%) with no treatment	P value not reported Reported as not significant for myringotomy *v* no treatment	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[22] RCT **4-armed trial**	171 children, aged 2 to 12 years with AOM The third arm evaluated amoxicillin (250 mg three times daily for 7 days) only The fourth arm evaluated amoxicillin plus myringotomy	**Pain , 7 days** 31/35 (89%) with myringotomy only 34/38 (90%) with no treatment	P value not reported Reported as not significant for myringotomy *v* no treatment	⟷	Not significant

Recurrence

No data from the following reference on this outcome. [22]

Complications

No data from the following reference on this outcome. [22]

Adverse effects

No data from the following reference on this outcome. [22]

Myringotomy versus antibiotics:

We found no systematic review but found three RCTs. [23] [22] [24]

Symptoms of AOM

Compared with antibiotics Myringotomy may be less effective at reducing symptoms of AOM after 12 hours to 11 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptoms of AOM					
[23] RCT **3-armed trial**	105 infants aged 3 months to 1 year with AOM The remaining arm evaluated myringotomy plus antibiotic (amoxicillin–clavulanic acid [co-amoxiclav])	**Persistent ear infection , 9 to 11 days** 21/30 (70%) with myringotomy plus placebo 2/30 (7%) with antibiotic (amoxicillin–clavulanic acid) 60 children in this analysis	P <0.001	○○○	antibiotic
[23] RCT **3-armed trial**	105 infants aged 3 months to 1 year with AOM	**Persistent ear infection , 3 to 6 days** 28/35 (80%) with myringotomy plus placebo	P <0.0001	○○○	antibiotic

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	The remaining arm evaluated myringotomy plus antibiotic (amoxicillin–clavulanic acid)	11/35 (31%) with antibiotic (amoxicillin–clavulanic acid) 70 children in this analysis			
[22] RCT **4-armed trial**	171 children aged 2 to 12 years with AOM The remaining arms evaluated amoxicillin plus myringotomy and no treatment	**No pain , 24 hours** 26/36 (72.2%) with myringotomy 34/47 (72.3%) with amoxicillin (250 mg three times daily for 7 days) 83 children in this analysis	P value not reported Reported as not significant for myringotomy *v* amoxicillin alone	⟷	Not significant
[22] RCT **4-armed trial**	171 children aged 2 to 12 years with AOM The remaining arms evaluated amoxicillin plus myringotomy and no treatment	**No pain , 7 days** 31/35 (89%) with myringotomy 43/46 (93%) with amoxicillin (250 mg three times daily for 7 days) 81 children in this analysis	P value not reported Reported as not significant	⟷	Not significant
[24] RCT **3-armed trial**	83 episodes of AOM in children, aged 2 to 12 years with severe AOM or recurrent AOM The remaining arm evaluated myringotomy plus amoxicillin	**Initial treatment failure , 12 hours** 23% with myringotomy plus placebo 4% with amoxicillin (40 mg/kg/day in 3 divided doses for 14 days) Absolute numbers not reported	P = 0.006 Results include severe episodes of AOM in children aged 2 to 12 years only	○○○	amoxicillin

Recurrence

No data from the following reference on this outcome. [23] [22] [24]

Complications

No data from the following reference on this outcome. [23] [22] [24]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[23] RCT **3-armed trial**	105 infants, aged 3 months to 1 year with AOM	**Loose or watery bowel movements** 0/30 (0%) with myringotomy plus placebo 7/60 (12%) with antibiotic (amoxicillin–clavulanic acid)	P = 0.05	○○○	myringotomy plus placebo

No data from the following reference on this outcome. [22] [24]

Further information on studies

[22] The RCT provided results in the form of children or as individual ears as the unit measured. Because randomisation was based on children, the figures reported here exclude those results based on individual ears.

[23] AOM was defined as the presence of middle-ear effusion and bulging (with or without redness of the tympanic membrane) associated with recent irritability or fever. The RCT provided results in the form of children or as individual ears as the unit measured. Because randomisation was based on children, the figures reported here exclude those results based on individual ears.

[24] AOM was diagnosed on the basis of fever, ear ache, or irritability with redness and/or bulging of the eardrum. An episode of AOM was classified as severe or non-severe according to the child's temperature and an ear ache score.

Comment: None.

QUESTION What are the effects of interventions to prevent recurrence of AOM in children?

OPTION ANTIBIOTIC PROPHYLAXIS (LONG TERM)

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Long-term antibiotic prophylaxis may reduce recurrence rates; however, the possibility of adverse effects and antibiotic resistance should be taken into account.
- We do not know whether any one regimen should be used in preference to another to prevent recurrent attacks.

Benefits and harms

Antibiotic prophylaxis versus placebo:

We found one systematic review (13 RCTs, search date 2006), which compared antibiotics versus placebo or no treatment for the prevention of AOM, AOM with perforation, or chronic suppurative otitis media. [25]

Recurrence

Compared with placebo Prophylactic antibiotics are more effective at reducing the incidence of AOM compared with placebo or no treatment in children at risk of otitis media (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[25] Systematic review	1358 children at increased risk of AOM 13 RCTs in this analysis	**Proportion of children with AOM or chronic suppurative otitis media** 253/748 (34%) with antibiotics 331/610 (54%) with placebo or no treatment	RR 0.62 95% CI 0.52 to 0.75	●○○	antibiotics
[25] Systematic review	1112 children at increased risk of AOM 12 RCTs in this analysis	**Number of episodes of otitis media** 360 episodes with antibiotics 752 episodes with placebo or no treatment	Incidence rate ratio (IRR) 0.48 95% CI 0.37 to 0.62; see further information on studies for definition of IRR Antibiotics prevented 1.5 episodes of AOM for every 12 months of treatment per child	○○○	antibiotics

Symptoms of AOM

No data from the following reference on this outcome. [25]

Complications

No data from the following reference on this outcome. [25]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[25] Systematic review	714 children at increased risk of AOM 11 RCTs in this analysis	**Adverse effects** 10/405 (2%) with antibiotics 3/309 (1%) with placebo or no treatment	RR 1.99 95% CI 0.25 to 15.89	⟷	Not significant

Further information on studies

[25] The incidence rate ratio (IRR), also known as the rate ratio, is the incidence rate in the intervention group divided by the incidence rate in the placebo group.

Comment: **Clinical guide:**
We found insufficient evidence on which antibiotic to use and for how long, and on how many episodes of AOM to justify starting preventive treatment.

OPTION PNEUMOCOCCAL VACCINE

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Vaccination in infancy with pneumococcal conjugate vaccine (PCV) has some effect on recurrent AOM.
- Vaccination with PCV in children aged 1 to 7 years with recurrent AOM has no effect on recurrences.
- The adverse effects associated with pneumococcal vaccination are unclear.
- **Note**
  We found no clinically important results from RCTs about the effects of the 23-valent pneumococcal vaccine that is currently available.

Benefits and harms

Pneumococcal vaccine versus placebo or control:

We found one systematic review (search date 2007). [26] The review included 7 RCTs on 7- to 11-valent pneumococcal conjugate vaccine (PCV) (with different carrier proteins). Owing to significant heterogeneity regarding study population, type of conjugate vaccine, and outcome measures, the review did not perform a meta-analysis. We therefore present results from individual RCTs.

Recurrence

Compared with placebo or control vaccine Pneumococcal conjugate vaccine (7- to 11-valent) may be more effective than placebo at reducing the incidence of AOM when administered during infancy, but may be no more effective when given to children aged 1 to 7 years with recurrent AOM (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[26] Systematic review	37,868 children aged 2 months Data from 1 RCT	**Episodes , per person-year** with vaccination with control vaccine Absolute results not reported Intention-to-treat analysis	Relative risk reduction (RRR) 6% 95% CI 4% to 8%	○○○	pneumococcal vaccine
[26] Systematic review	1662 children aged 2 months Data from 1 RCT	**Episodes , per person-year** 1.16 with vaccination 1.24 with control vaccine Per-protocol analysis	RRR +6% 95% CI –4% to +16%	⟷	Not significant
[26] Systematic review	1666 children aged 2 months Data from 1 RCT	**Episodes , per person-year** with vaccination with control vaccine Absolute results not reported Per-protocol analysis	RRR –1% 95% CI –12% to +10%	⟷	Not significant
[26] Systematic review	4968 children aged 6 weeks to 5 months Data from 1 RCT	**Episodes , per person-year** 0.08 with vaccination 0.13 with control vaccine Per-protocol analysis	RRR 34% 95% CI 21% to 44%	○○○	pneumococcal vaccine
[26] Systematic review	264 children aged 12 months to 35 months Data from 1 RCT	**Episodes , per person-year** 0.66 with vaccination 0.79 with control vaccine Intention-to-treat analysis	RRR +17% 95% CI –2% to +33%	⟷	Not significant
[26] Systematic review	383 children aged 1 year to 7 years with recurrent AOM Data from 1 RCT	**Episodes , per person-year** 1.1 with vaccination 0.83 with control vaccine Intention-to-treat analysis	RRR –29% 95% CI –62% to –2%	○○○	control vaccine
[26] Systematic review	74 children aged 1 year to 7 years with recurrent AOM Data from 1 RCT	**Episodes , per person-year** 0.78 with vaccination 0.67 with control vaccine Per-protocol analysis	RRR –16% 95% CI –96% to +31%	⟷	Not significant
[26] Systematic review	37,868 children aged 2 months Data from 1 RCT	**Recurrent AOM** with vaccination with control vaccine Absolute results not reported Recurrent AOM was defined as at least 3 episodes in 6 months or at least 4 episodes in 1 year Intention-to-treat analysis	RRR 9% 95% CI 4% to 14%	○○○	pneumococcal vaccine
[26] Systematic review	1662 children aged 2 months Data from 1 RCT	**Recurrent AOM** with vaccination with control vaccine	RRR +9% 95% CI –12% to +27%	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute results not reported Recurrent AOM was defined as at least 3 episodes in 6 months or at least 4 episodes in 1 year Intention-to-treat analysis			
[26] Systematic review	4968 children aged 6 weeks to 5 months Data from 1 RCT	**Recurrent AOM** with vaccination with control vaccine Absolute results not reported Recurrent AOM was defined as at least 3 episodes in 6 months or at least 4 episodes in 1 year Per-protocol analysis	RRR +56% 95% CI –2% to +81%	⟷	Not significant

Symptoms of AOM

No data from the following reference on this outcome. [26]

Complications

No data from the following reference on this outcome. [26]

Adverse effects

No data from the following reference on this outcome. [26]

Further information on studies

Comment: **Clinical guide:**
Based on the current evidence, the review concluded that pneumococcal conjugate vaccine (PCV) is marginally beneficial in preventing AOM in infancy. The discrete reductions of 6% may, however, result in substantial reductions from a public health perspective. In most western countries, PCVs are implemented in national childhood vaccination programmes because of the effect on invasive pneumococcal infections. Administering PCVs in older children with a history of AOM has no effect on preventing further AOM episodes.

OPTION TYMPANOSTOMY (VENTILATION TUBES)

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Tympanostomy with ventilation tube insertion leads to short-term reduction in the number of episodes of AOM, but it increases the risk of complications.

- We found limited evidence of only a short-term benefit from tympanostomy with ventilation tubes, with possibly increased risks of tympanosclerosis.
- Tympanostomy plus drainage tubes may increase the risk of tympanosclerosis and hearing impairment.

Benefits and harms

Tympanostomy versus no surgery or myringotomy alone:

We found one systematic review (search date 2008) [27] and one additional RCT. [28]

Recurrence

Compared with no surgery or myringotomy alone Tympanostomy plus insertion of drainage tubes may be more effective at reducing the incidence of AOM after 6 months, but not after 18 months (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[27] Systematic review	148 children aged <3 years 2 RCTs in this analysis	**Proportion of children with at least 1 episode of AOM , 6 months** 40/85 (47%) with tympanostomy 51/63 (81%) with control	OR 0.18 95% CI 0.08 to 0.42	●●●	tympanostomy
[28] RCT	44 children, aged 9 months to 7 years, with bilateral recurrent AOM of equal severity in each ear despite >3 months of antibiotic prophylaxis	**Mean number of episodes of AOM , 6 months** 0.6% with tympanostomy tube insertion into a randomly selected ear 1.8% with contralateral ear receiving either no surgery or myringotomy alone Absolute numbers not reported	Difference in mean number of episodes: –1.2 95% CI –2.2 to –0.9	○○○	tympanostomy
[28] RCT	44 children, aged 9 months to 7 years, with bilateral recurrent AOM of equal severity in each ear despite >3 months of antibiotic prophylaxis	**Mean number of episodes of AOM , 18 months** 0.8% with tympanostomy tube insertion into a randomly selected ear 0.8% with contralateral ear receiving either no surgery or myringotomy alone Absolute numbers not reported	Difference in mean number of episodes 0% 95% CI –0.3 to +0.3	⟷	Not significant
[28] RCT	44 children, aged 9 months to 7 years, with bilateral recurrent AOM of equal severity in each ear despite >3 months of antibiotic prophylaxis	**Recurrent ear infections** with tympanostomy tube insertion into a randomly selected ear with contralateral ear receiving either no surgery or myringotomy alone Absolute results not reported	P = 0.3 The RCT reported a non-significant trend towards more recurrent infections and worse hearing in ears that had received tympanostomy tubes, which became apparent after tube extrusion	⟷	Not significant

Complications

Compared with no surgery or myringotomy alone Tympanostomy plus insertion of drainage tubes may increase the risk of tympanosclerosis in children with AOM (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Tympanosclerosis					
[28] RCT	44 children, aged 9 months to 7 years with bilateral recurrent AOM of equal severity in each ear despite >3 months of antibiotic prophylaxis	**Tympanosclerosis** 35/61 (57%) with tympanostomy tube 5/26 (19%) with myringotomy alone	P = 0.004	○○○	myringotomy alone
[28] RCT	44 children, aged 9 months to 7 years with bilateral recurrent AOM of equal severity in each ear despite >3 months of antibiotic prophylaxis	**Tympanosclerosis** 35/61 (57%) with tympanostomy tube 2/27 (7%) with no surgery	P less than or equal to 0.0001	○○○	no surgery

No data from the following reference on this outcome. [27]

Symptoms of AOM

No data from the following reference on this outcome. [27] [28]

Adverse effects

No data from the following reference on this outcome. [27] [28]

Further information on studies

[27] The review included only studies that randomised children and excluded the RCT that randomised ears. [28]

[28] Recurrent AOM was defined as the recurrent presence (>4 episodes) of ear ache with red and bulging tympanic membranes. Anatomical abnormalities (tympanosclerosis, atrophy, or retraction and chronic perforation), although not thought to be clinically significant, were more common in the ears receiving tympanostomy tubes. The RCT included some children with otitis media with effusion, although the results concerning benefits presented here refer only to those children in the study with recurrent AOM. It was not possible from the data available to differentiate the evidence on harms into children with recurrent AOM compared with otitis media with effusion. Medical treatment and antibiotic prophylaxis were allowed "whenever indicated". It was not possible from the data presented to tell whether the different groups differed in the amount of medical treatment and prophylactic antibiotics.

Comment: None.

OPTION INFLUENZA VACCINE New

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Influenza vaccination in healthy children has no effect on the incidence of AOM.

Benefits and harms

Influenza vaccine versus placebo:

We found one systematic review (search date 2007, 6 RCTs). [29]

Recurrence

Compared with placebo Influenza vaccine seems no more effective at preventing incidence of AOM in children aged 6 months to 7 years (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[29] Systematic review	5253 children aged 6 months to 7 years 6 RCTs in this analysis	**Incidence of AOM , 3 to 8 months** 1249/3223 (39%) with influenza vaccination 832/2030 (41%) with placebo	RR 1.00 95% CI 0.79 to 1.26 P = 0.99	⟷	Not significant

Symptoms of AOM

No data from the following reference on this outcome. [29]

Complications

No data from the following reference on this outcome. [29]

Adverse effects

No data from the following reference on this outcome. [29]

Further information on studies

Comment: The RCTs in the systematic review [29] included only healthy children; therefore, we can draw no firm conclusions about children with recurrent AOM.

OPTION XYLITOL SYRUP OR GUM New

- For GRADE evaluation of interventions for AOM in children, see table, p 29 .
- Xylitol must be given as prophylaxis, not as treatment.
- Xylitol chewing gum or syrup given 5 times daily has a small preventive effect on recurrence of AOM, but the compliance issues in giving a medicine to such young children 5 times daily render it an unrealistic treatment option.
- Xylitol is not effective when given 3 times daily or only during an acute respiratory tract infection.

Benefits and harms

Xylitol versus placebo:

We found no systematic review, but found 4 RCTs. [30] [31] [32] [33]

Recurrence

Compared with placebo Xylitol given 5 times daily, but not 3 times daily, may be more effective at reducing recurrence of AOM in children aged up to 7 years. Xylitol may be no more effective at reducing AOM recurrence when given only during an acute respiratory tract infection (low-quality evidence). **Note** The issues of compliance in giving a medicine to such young children 5 times daily render xylitol an unrealistic treatment option.

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence of AOM					
[30] RCT	306 children with recurrent AOM, mean age 5 years	**Children with at least one episode of AOM , 2 months** 19/157 (12%) with xylitol 31/149 (21%) with control (sucrose) Treatment or control given 5 times daily as a chewing gum	ARR 8.7% 95% CI 0.4% to 17.0% P = 0.04	○○○	xylitol chewing gum
[31] RCT **5-armed trial**	857 children with recurrent AOM The remaining arms assessed xylitol chewing gum, control chewing gum, and xylitol lozenge	**Incidence rate of AOM per person-years at risk , 3 months** 2.01 with xylitol syrup 3.03 with control syrup 324 children in this analysis, mean age 2.2 years Treatment and control given 5 times daily as a syrup	Difference 1.02 95% CI 0.29 to 1.75 P = 0.006	○○○	xylitol syrup
[31] RCT **5-armed trial**	857 children with recurrent AOM The remaining arms assessed xylitol syrup, control syrup, and xylitol lozenge	**Incidence rate of AOM per person-years at risk , 3 months** 1.04 with xylitol chewing gum 1.69 with control chewing gum 357 children in this analysis, mean age 4.6 years Treatment and control given 5 times daily as a chewing gum	Difference 0.65 95% CI 0.14 to 1.16 P = 0.012	○○○	xylitol chewing gum
[32] RCT **5-armed trial**	1277 children with recurrent AOM during an acute respiratory tract infection The remaining arms assessed xylitol chewing gum, control chewing gum, and xylitol lozenges	**Children with AOM , 3 weeks** 34/166 (20.5%) with xylitol syrup 32/157 (20.4%) with control syrup 323 children in this analysis, mean age 3.6 years Treatment or control given 5 times daily as a syrup, only during the acute respiratory tract infection	ARR –0.1 95% CI –8.3 to +5.8 P = 0.72	⟷	Not significant
[32] RCT **5-armed trial**	1277 children with recurrent AOM during an acute respiratory tract infection The remaining arms assessed xylitol syrup, control syrup, and xylitol lozenges	**Children with AOM , 3 weeks** 31/220 (14%) with xylitol chewing gum 24/218 (11%) with control chewing gum 438 children in this analysis, mean age 4.8 years Treatment or control given 5 times daily as a chewing gum, only during the acute respiratory tract infection	ARR –0.1 95% CI –9.4 to +3.2 P = 0.33	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[33] RCT	663 children with recurrent AOM, mean age 4.1 years	**Incidence rate of AOM per person-years at risk , 3 months** 2.09 with xylitol 1.83 with control Treatment and control given 3 times daily as either a chewing gum or syrup, depending on whether the child was old enough to chew gum	Difference –0.26 95% CI –0.71 to +0.19 P = 0.25	⟷	Not significant

Symptoms of AOM

No data from the following reference on this outcome. [30] [31] [32] [33]

Complications

No data from the following reference on this outcome. [30] [31] [32] [33]

Adverse effects

No data from the following reference on this outcome. [30] [31] [32] [33]

Further information on studies

Comment: Compliance is a potential problem with a medication that must be given 5 times a day to a young child. In addition, the preventing effect of xylitol is quite small — only one episode of AOM per year. For the time being, then, xylitol does not represent a realistic treatment option for AOM in children.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Mastoiditis The presence of infection in the mastoid cavity.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Myringotomy The surgical creation of a perforation in the tympanic membrane.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Influenza vaccine New option added. Categorised as Unlikely to be beneficial.

Xylitol syrup or gum New option added. Categorised as Unlikely to be beneficial.

Analgesics for AOM in children One Cochrane systematic review updated. [10] Categorisation unchanged (Likely to be beneficial).

Antibiotic prophylaxis for preventing recurrence of AOM in children One Cochrane systematic review updated. [25] Categorisation unchanged (Trade-off between benefits and harms).

Antibiotics versus placebo for AOM in children New evidence added. [13] [14] Categorisation unchanged (Trade-off between benefits and harms).

Choice of antibiotic regimen New evidence added. [18] Categorisation unchanged (Trade-off between benefits and harms).

Immediate or delayed antibiotics for AOM in children New evidence added. [19] Categorisation unchanged (Trade-off between benefits and harms).

Longer versus shorter courses of antibiotics One Cochrane systematic review updated. [21] Categorisation unchanged (Trade-off between benefits and harms).

Tympanostomy (ventilation tubes) New evidence added. [27] Categorisation unchanged (Likely to be ineffective or harmful).

Pneumococcal vaccine New evidence added. [26] Categorisation changed from Unlikely to be beneficial to Likely to be beneficial.

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Disclaimer

GRADE **Evaluation of interventions for AOM in children.**

Important outcomes			Complications, Recurrence, Symptoms of AOM						
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatments for AOM in children?									
2 (117) [10]	Symptoms of AOM	Topical anaesthetic versus placebo	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of studies that included oral analgesics
1 (219) [11]	Symptoms of AOM	Oral analgesics versus placebo	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for uncertain validity of outcome assessment
at least 19 (at least 3805) [12] [13] [15]	Symptoms of AOM	Antibiotics versus placebo	4	0	–1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for range of interventions included
6 (2153) [13]	Recurrence	Antibiotics versus placebo	4	0	0	0	0	High	
1 (2287) [13] [14]	Complications	Antibiotics versus placebo	4	0	0	–1	0	Moderate	Directness point deducted for range of interventions included
at least 27 (at least 4580) [17] [2] [18]	Symptoms of AOM	Different antibiotics versus each other	4	–2	0	–2	0	Very low	Quality points deducted for incomplete reporting of results and heterogeneity of outcome measures and controls. Directness points deducted for range of participants and interventions included
2 (498) [19]	Symptoms of AOM	Immediate versus delayed antibiotic treatment	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
27 (6727) [21]	Symptoms of AOM	Longer versus shorter course of antibiotics	4	0	0	0	0	High	
1 (171) [22]	Symptoms of AOM	Myringotomy versus no myringotomy	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
3 (821) [23] [22] [24]	Symptoms of AOM	Myringotomy versus antibiotics	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results
What are the effects of interventions to prevent recurrence of AOM in children?									
13 (at least 1358) [25]	Recurrence	Antibiotic prophylaxis versus placebo	4	0	0	0	0	High	
12 (46,457) [26]	Recurrence	Pneumococcal vaccine versus placebo or control	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting and for no intention-to-treat analyses in many RCTs. Consistency point deducted for conflicting results
3 (192) [27] [28]	Recurrence	Tympanostomy versus no surgery or myringotomy alone	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for different results at different end points
1 (44) [28]	Complications	Tympanostomy versus no surgery or myringotomy alone	4	–1	–1	0	0	Low	Quality point deducted for sparse data. Consistency point deducted for different results at different end points

Important outcomes			Complications, Recurrence, Symptoms of AOM						
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
6 (5253) [29]	Recurrence	Influenza vaccine versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for poor methodology (vaccination completed after the beginning of viral circulation in 1 large RCT)
4 (2411) [30] [31] [32] [33]	Recurrence	Xylitol versus placebo	4	0	–1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for range of interventions
We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.									